

**IN THE CLAIMS:**

Claims 1-12. (canceled)

13. (new) Oligonucleotides selected from the group comprising SEQ ID NO 3 and elongated sequences of SEQ ID NO 3 which can be represented by the following general formula:



wherein X is selected from the group comprising the following oligonucleotides:

ACAGGACGATGTGCAGCGGCCACAGGCCCCTGAG,  
CAGGACGATGTGCAGCGGCCACAGGCCCCTGAG,  
AGGACGATGTGCAGCGGCCACAGGCCCCTGAG,  
GGACGATGTGCAGCGGCCACAGGCCCCTGAG,  
GACGATGTGCAGCGGCCACAGGCCCCTGAG,  
ACGATGTGCAGCGGCCACAGGCCCCTGAG,  
CGATGTGCAGCGGCCACAGGCCCCTGAG,  
GATGTGCAGCGGCCACAGGCCCCTGAG,  
ATGTGCAGCGGCCACAGGCCCCTGAG, TGTGCAGCGGCCACAGGCCCCTGAG,  
GTGCAGCGGCCACAGGCCCCTGAG, TGCAGCGGCCACAGGCCCCTGAG,  
GCAGCGGCCACAGGCCCCTGAG, CAGCGGCCACAGGCCCCTGAG,  
AGCGGCCACAGGCCCCTGAG, GCGGCCACAGGCCCCTGAG,  
CGGCCACAGGCCCCTGAG, GGCCACAGGCCCCTGAG, GCCACAGGCCCCTGAG,  
CCACAGGCCCCTGAG, CACAGGCCCCTGAG, ACAGGCCCCTGAG,  
CAGGCCCCTGAG, AGGCCCCTGAG, GGCCCCTGAG, GCCCCTGAG, CCCCTGAG,  
CCCTGAG, CCTGAG, CTGAG, TGAG, GAG, AG, G,

and wherein Z is selected from the group comprising the following oligonucleotides:

GCAGACCCCGCTGCTCGTCATAGACCGAGCCCC,  
GCAGACCCCGCTGCTCGTCATAGACCGAGCCCC,

GCAGACCCCGCTGCTCGTCATAGACCGAGCCC,  
 GCAGACCCCGCTGCTCGTCATAGACCGAGCC,  
 GCAGACCCCGCTGCTCGTCATAGACCGAGC,  
 GCAGACCCCGCTGCTCGTCATAGACCGAG,  
 GCAGACCCCGCTGCTCGTCATAGACCGA,  
 GCAGACCCCGCTGCTCGTCATAGACCG,  
 GCAGACCCCGCTGCTCGTCATAGACC, GCAGACCCCGCTGCTCGTCATAGAC,  
 GCAGACCCCGCTGCTCGTCATAGA, GCAGACCCCGCTGCTCGTCATAG,  
 GCAGACCCCGCTGCTCGTCATA, GCAGACCCCGCTGCTCGTCAT,  
 GCAGACCCCGCTGCTCGTCA, GCAGACCCCGCTGCTCGTC,  
 GCAGACCCCGCTGCTCGT, GCAGACCCCGCTGCTCG, GCAGACCCCGCTGCTC,  
 GCAGACCCCGCTGCT, GCAGACCCCGCTGC, GCAGACCCCGCTG,  
 GCAGACCCCGCT, GCAGACCCCGC, GCAGACCCCG, GCAGACCCC,  
 GCAGACCC, GCAGACC, GCAGAC, GCAGA, GCAG, GCA, GC, G,

and wherein X and Z together comprise not more than 34 nucleobases and mimetics thereof

wherein said oligonucleotides are capable of hybridizing sufficiently with the region encompassing the translation initiation codon of the open reading frame of the gene encoding TGF-R<sub>II</sub>, and mimetics, variants, salts and optical isomers of said sequence

and with the proviso that said oligonucleotide is not  
 5'-CAGCCCCCGACCCATGGCAG-3'.

14. (new) Oligonucleotides selected from the group comprising SEQ ID NO 3 to SEQ ID NO 32 and SEQ ID NO 34 to SEQ ID NO 72

wherein said oligonucleotides are capable of hybridizing sufficiently with the region encompassing the translation initiation or termination codon of the open reading frame of the gene encoding TGF-R<sub>II</sub>, or a region of the mRNA encoding TGF-R<sub>II</sub> which is a "loop" or "bulge" and which is not part of a secondary structure and mimetics, variants, salts and

optical isomers of said sequence.

15. (new) Oligonucleotides according to claim 14 selected from the group comprising:

SEQ ID NO 3:5'-CAGCCCCCGACCCATG-3'

SEQ ID NO 34:5'-CAGCCCCCGACCCATGGCA-3'

SEQ ID NO 35:5'-CAGCCCCCGACCCATGGC-3'

SEQ ID NO 36:5'-CAGCCCCCGACCCATGG-3'

SEQ ID NO 41:5'-GCAGCCCCCGACCCATGGCA-3'

SEQ ID NO 42:5'-GCAGCCCCCGACCCATGGC-3'

SEQ ID NO 43:5'-GCAGCCCCCGACCCATGG-3'

SEQ ID NO 44:5'-GCAGCCCCCGACCCATG-3'

SEQ ID NO 49:5'-AGCAGCCCCCGACCCATGGC-3'

SEQ ID NO 50:5'-AGCAGCCCCCGACCCATGG-3'

SEQ ID NO 51:5'-AGCAGCCCCCGACCCATG-3'

SEQ ID NO 56:5'-GAGCAGCCCCCGACCCATGG-3'

SEQ ID NO 57:5'-GAGCAGCCCCCGACCCATG-3'

SEQ ID NO 62:5'-TGAGCAGCCCCCGACCCATG-3'.

16. (new) Pharmaceutical preparation comprising at least one oligonucleotide according to claim 13 as well as mimetics, variants, salts and optical isomers thereof and/or at least one antisense compound comprising a vector allowing to transcribe at least one said oligonucleotide together with at least one pharmaceutically acceptable carrier, excipient or diluents.
17. (new) Pharmaceutical preparation according to claim 16, wherein the pharmaceutical preparation is an infusion solution or a solid matrix for continuous release of the active ingredient.
18. (new) Pharmaceutical preparation according to claim 16, wherein the pharmaceutical preparation is suitable for local administration into the brain.

19. (new) Use of at least one oligonucleotide having a sequence at least 80% identical to a sub-sequence of SEQ ID NO 1 or SEQ ID NO 2 comprising 8 to 50 nucleobases, wherein said sequence is capable of hybridizing sufficiently with the region encompassing the translation initiation or termination codon of the open reading frame of the gene encoding TGF-R<sub>II</sub>, or a region of the mRNA encoding TGF-R<sub>II</sub> which is a "loop" or "bulge" and which is not part of a secondary structure and mimetics, variants, salts and optical isomers of said sequence for promoting successful regeneration and functional reconnection of damaged neural pathways.
20. (new) Use of at least one oligonucleotide according to claim 19 as well as mimetics and variants thereof and/or at least one antisense compound comprising a vector allowing to transcribe at least one said oligonucleotide or a pharmaceutical formulation comprising at least one oligonucleotide according to claim 7 for promoting successful regeneration and functional reconnection of damaged neural pathways.
21. (new) Use of at least one oligonucleotide according to claim 20 as well as mimetics and variants thereof and/or at least one antisense compound comprising a vector allowing to transcribe at least one said oligonucleotide or a pharmaceutical formulation comprising at least one oligonucleotide according to claim 7 for prophylaxis, therapeutic prevention and treatment of neurodegenerative, traumatic / posttraumatic, vascular/hypoxic, neuroinflammatory and postinfectious Central Nervous System disorders, as well as age induced decreases in neuronal stem cell renewal.
22. (new) Use according to claim 21 for inhibiting TGF-R<sub>II</sub> expression in diseases associated with up-regulated or enhanced TGF-R<sub>II</sub> levels.
23. (new) Use according to claim 21, wherein the diseases associated with up-regulated or enhanced TGF-R<sub>II</sub> levels or the neurodegenerative disorders and neuroinflammatory disorders are selected from the group comprising: Alzheimer's diseases, Parkinson's

disease, Creutzfeldt Jakob disease (CJD), new variant of Creutzfeldt Jakobs disease (nvCJD), Hallervorden Spatz disease, Huntington's disease, Multisystem Atrophy, Dementia, Frontotemporal Dementia, Amyotrophic Lateral Sclerosis, Spinal Muscular Atrophy, Spinocerebellar Atrophies (SCAs), or other Motor Neuron Disorders, schizophrenia, affective disorders, major depression, meningoencephalitis, bacterial meningoencephalitis, viral meningoencephalitis, CNS autoimmune disorders, Multiple Sclerosis (MS), acute ischemic / hypoxic lesions, stroke, CNS and spinal cord trauma, head and spinal trauma, arteriosclerosis, atherosclerosis, microangiopathic dementia, Binswanger' disease (Leukoaraiosis), retinal degeneration, cochlear degeneration, macular degeneration, cochlear deafness, AIDS-related dementia, retinitis pigmentosa, fragile X-associated tremor/ataxia syndrome (FXTAS), progressive supranuclear palsy (PSP), striatonigral degeneration (SND), olivopontocerebellar degeneration (OPCD), Shy Drager syndrome (SDS), age dependant memory deficits, neurodevelopmental disorders associated with dementia, Down's Syndrome, synucleinopathies, Superoxide Dismutase Mutations, Trinucleotide Repeat Disorders, trauma, hypoxia, vascular diseases, vascular inflammations, CNS-ageing.

24. (new) Use according to claim 21 for inhibiting TGF- $\beta$  activity in diseases associated with up-regulated or enhanced signaling of TGF-R<sub>II</sub>.
25. (new) Use according to claim 21, wherein the diseases associated with up-regulated or enhanced signaling of TGF-R<sub>II</sub> or the neurodegenerative disorders and neuroinflammatory disorders are selected from the group comprising: Alzheimer's diseases, Parkinson's disease, Creutzfeldt Jakob disease (CJD), new variant of Creutzfeldt Jakobs disease (nvCJD), Hallervorden Spatz disease, Huntington's disease, Multisystem Atrophy, Dementia, Frontotemporal Dementia, Amyotrophic Lateral Sclerosis, Spinal Muscular Atrophy, Spinocerebellar Atrophies (SCAs), or other Motor Neuron Disorders, schizophrenia, affective disorders, major depression, meningoencephalitis, bacterial meningoencephalitis, viral meningoencephalitis, CNS autoimmune disorders, Multiple Sclerosis (MS), acute ischemic / hypoxic lesions, stroke, CNS and spinal cord trauma, head

and spinal trauma, arteriosclerosis, atherosclerosis, microangiopathic dementia, Binswanger' disease (Leukoaraiosis), retinal degeneration, cochlear degeneration, macular degeneration, cochlear deafness, AIDS-related dementia, retinitis pigmentosa, fragile X-associated tremor/ataxia syndrome (FXTAS), progressive supranuclear palsy (PSP), striatonigral degeneration (SND), olivopontocerebellar degeneration (OPCD), Shy Drager syndrome (SDS), age dependant memory deficits, neurodevelopmental disorders associated with dementia, Down's Syndrome, synucleinopathies, Superoxide Dismutase Mutations, Trinucleotide Repeat Disorders, trauma, hypoxia, vascular diseases, vascular inflammations, CNS-ageing.

26. (new) Method for identifying a compound interfering with (a) the biological activity of TGF- $R_{II}$  or the expression of TGF- $R_{II}$ , or (b) the TGF- $\beta 1$ /TGF-R signaling, comprising the steps of:
- (a) incubating a candidate compound with a test system comprising TGF- $\beta 1$  and neuronal precursor cells; and
  - (b) assaying the expression of active TGF receptors or the proliferation of the neuronal precursor cells;
- wherein
- (c) an abolition of (i) the suppression of expression of active TGF receptors or (ii) suppression of proliferation of the neuronal precursor cells compared to the test system in the absence of said test compound is indicative of the presence of a candidate compound having the desired properties.
27. (new) Oligonucleotides having a sequence at least 80% identical to a sub-sequence of SEQ ID NO 94 or SEQ ID NO 95 or SEQ ID NO 96 comprising 8 to 50 nucleobases, wherein said sequence is capable of hybridizing sufficiently with the region encompassing the translation initiation or termination codon of the open reading frame of the gene encoding TGF- $R_I$ , or a region of the mRNA encoding TGF- $R_I$  which is a "loop" or "bulge" and which is not part of a secondary structure and mimetics, variants, salts and optical isomers of said sequence.

28. (new) Oligonucleotides having a sub-sequence of SEQ ID NO 94 or SEQ ID NO 95 or SEQ ID NO 96 comprising 8 to 50 nucleobases and mimetics, variants, salts and optical isomers thereof.

29. (new) Oligonucleotides according to claim 28, selected from the group comprising

SEQ ID NO 73:5'-ATGTGAAGATGGGCAAGACC-3'

SEQ ID NO 74:5'-ATCTCCATGTGAAGATGGGC-3'

SEQ ID NO 75:5'-AACGGCCTATCTCGAGGAAT-3'

SEQ ID NO 76:5'-AACATCGTCGAGCAATTTCC-3'

SEQ ID NO 77:5'-AATCCAACCTCCTTTGCCCTT-3'

SEQ ID NO 78:5'-AAACCTGAGCCAGAACCTGA-3'

SEQ ID NO 79:5'-AGGGCGATCTAATGAAGGGT-3'

SEQ ID NO 80:5'-AGTGCACAGAAAGGACCCAC-3'

SEQ ID NO 81:5'-ACACTGGTCCAGCAATGACA-3'

SEQ ID NO 82:5'-TTCCTGTTGACTGAGTTGCG-3'

SEQ ID NO 83:5'-CACTCTGTGGTTTGGAGCAA-3'

SEQ ID NO 84:5'-CAAGGCCAGGTGATGACTTT-3'

SEQ ID NO 85:5'-CACACTGGTCCAGCAATGAC-3'

SEQ ID NO 86:5'-CTGACACCAACCAGAGCTGA-3'

SEQ ID NO 87:5'-CTCTGCCATCTGTTTGGGAT-3'

SEQ ID NO 88:5'-TCAAAAAGGGATCCATGCTC-3'

SEQ ID NO 89:5'-TGACACCAACCAGAGCTGAG-3'

SEQ ID NO 90:5'-TGATGCCTTCCTGTTGACTG-3'

SEQ ID NO 91:5'-TTCCTGTTGACTGAGTTGCG-3'

SEQ ID NO 92:5'-TTCTCCAAATCGACCTTTGC-3'

SEQ ID NO 93:5'-GGAGAGTTCAGGCAAAGCTG-3'.

30. (new) Pharmaceutical preparation comprising at least one oligonucleotide according to claim 27 as well as mimetics, variants, salts and optical isomers thereof and/or at least one

antisense compound comprising a vector allowing to transcribe at least one said oligonucleotide together with at least one pharmaceutically acceptable carrier, excipient or diluents.

31. (new) Pharmaceutical preparation according to claim 30, wherein the pharmaceutical preparation is an infusion solution or a solid matrix for continuous release of the active ingredient.
32. (new) Pharmaceutical preparation according to claim 30, wherein the pharmaceutical preparation is suitable for local administration into the brain.
33. (new) Use of at least one oligonucleotide according to claim 27 as well as mimetics and variants thereof and/or at least one antisense compound comprising a vector allowing to transcribe at least one said oligonucleotide or a pharmaceutical formulation according to claim 30 for promoting successful regeneration and functional reconnection of damaged neural pathways.
34. (new) Use of at least one oligonucleotide according to claim 27 as well as mimetics and variants thereof and/or at least one antisense compound comprising a vector allowing to transcribe at least one said oligonucleotide or a pharmaceutical formulation according to claim 18 for prophylaxis, therapeutic prevention and treatment of neurodegenerative, traumatic / posttraumatic, vascular/hypoxic, neuroinflammatory and postinfectious Central Nervous System disorders, as well as age induced decreases in neuronal stem cell renewal.
35. (new) Use according to claim 34 for inhibiting TGF-R<sub>I</sub> expression in diseases associated with up-regulated or enhanced signaling of TGF-R<sub>I</sub>.
36. (new) Use according to claim 34, wherein the neurodegenerative disorders and neuroinflammatory disorders are selected from the group comprising: Alzheimer's diseases, Parkinson's disease, Creutzfeldt Jakob disease (CJD), new variant of Creutzfeldt



Jakobs disease (nvCJD), Hallervorden Spatz disease, Huntington's disease, Multisystem Atrophy, Dementia, Frontotemporal Dementia, Amyotrophic Lateral Sclerosis, Spinal Muscular Atrophy, Spinocerebellar Atrophies (SCAs), or other Motor Neuron Disorders, schizophrenia, affective disorders, major depression, meningoencephalitis, bacterial meningoencephalitis, viral meningoencephalitis, CNS autoimmune disorders, Multiple Sclerosis (MS), acute ischemic / hypoxic lesions, stroke, CNS and spinal cord trauma, head and spinal trauma, arteriosclerosis, atherosclerosis, microangiopathic dementia, Binswanger' disease (Leukoaraiosis), retinal degeneration, cochlear degeneration, macular degeneration, cochlear deafness, AIDS-related dementia, retinitis pigmentosa, fragile X-associated tremor/ataxia syndrome (FXTAS), progressive supranuclear palsy (PSP), striatonigral degeneration (SND), olivopontocerebellar degeneration (OPCD), Shy Drager syndrome (SDS), age dependant memory deficits, neurodevelopmental disorders associated with dementia, Down's Syndrome, synucleinopathies, Superoxide Dismutase Mutations, Trinucleotide Repeat Disorders, trauma, hypoxia, vascular diseases, vascular inflammations, CNS-ageing.

37. (new) Use according to claim 34 for inhibiting TGF- $\beta$  activity in diseases associated with up-regulated or enhanced TGF- $\beta$  levels.
38. (new) Use according to claim 37, wherein the diseases associated with up-regulated or enhanced TGF- $\beta$  levels or the neurodegenerative disorders and neuroinflammatory disorders are selected from the group comprising: Alzheimer's diseases, Parkinson's disease, Creutzfeldt Jakob disease (CJD), new variant of Creutzfeldt Jakobs disease (nvCJD), Hallervorden Spatz disease, Huntington's disease, Multisystem Atrophy, Dementia, Frontotemporal Dementia, Amyotrophic Lateral Sclerosis, Spinal Muscular Atrophy, Spinocerebellar Atrophies (SCAs), or other Motor Neuron Disorders, schizophrenia, affective disorders, major depression, meningoencephalitis, bacterial meningoencephalitis, viral meningoencephalitis, CNS autoimmune disorders, Multiple Sclerosis (MS), acute ischemic / hypoxic lesions, stroke, CNS and spinal cord trauma, head and spinal trauma, arteriosclerosis, atherosclerosis, microangiopathic dementia,

and spinal trauma, arteriosclerosis, atherosclerosis, microangiopathic dementia, Binswanger' disease (Leukoaraiosis), retinal degeneration, cochlear degeneration, macular degeneration, cochlear deafness, AIDS-related dementia, retinitis pigmentosa, fragile X-associated tremor/ataxia syndrome (FXTAS), progressive supranuclear palsy (PSP), striatonigral degeneration (SND), olivopontocerebellar degeneration (OPCD), Shy Drager syndrome (SDS), age dependant memory deficits, neurodevelopmental disorders associated with dementia, Down's Syndrome, synucleinopathies, Superoxide Dismutase Mutations, Trinucleotide Repeat Disorders, trauma, hypoxia, vascular diseases, vascular inflammations, CNS-ageing.

39. (new) Method for identifying a compound interfering with (a) the biological activity of TGF- $R_I$  or the expression of TGF- $R_I$ , or (b) the TGF- $\beta_1$ /TGF-R signaling, comprising the steps of:
- (a) incubating a candidate compound with a test system comprising TGF- $\beta_1$  and neuronal precursor cells; and
  - (b) assaying the expression of active TGF receptors or the proliferation of the neuronal precursor cells;
- wherein
- (c) an abolition of (i) the suppression of expression of active TGF receptors or (ii) suppression of proliferation of the neuronal precursor cells compared to the test system in the absence of said test compound is indicative of the presence of a candidate compound having the desired properties.